Outcomes of a Rapid Deployment Aortic Valve Versus Its Conventional Counterpart: A Propensity-Matched Analysis

Wahlers, Thorsten C W ; Andreas, Martin ; Rahmanian, Parwis ; Candolfi, Pascal ; Zemanova, Barbora ; Giot, Christophe ; Ferrari, Enrico ; Laufer, Günther

Abstract: OBJECTIVE The aim of this study was to compare outcomes after rapid-deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (AVR) from two studies. METHODS Patients who underwent RDAVR (INTUITY valve) in the prospective, 5-year, single-arm multicenter TRITON study, or conventional AVR (Perimount Magna Ease valve) in the prospective Perimount Magna Ease postmarket study, were propensity score matched and compared for procedural, hemodynamic, safety, and clinical outcomes. RESULTS Matched RDAVR (n = 106) and conventional AVR (n = 106) patients had similar baseline characteristics (mean ± SD age, 72.8 ± 7.6 vs 72.5 ± 7.4 years; male 59.4% vs 61.3%) and procedures (concomitant procedures: 41.5% vs 50.9%). Mean ± SD aortic cross-clamp time was significantly shorter in RDAVR than AVR patients (51.8 ± 20.9 vs 73.9 ± 33.2 minutes; $P < 0.001$), as was mean cardiopulmonary bypass time (82.8 ± 34.2 vs 102.4 ± 41.7 minutes; $P < 0.001$). At 1 year, RDAVR patients showed significantly lower mean ± SD and peak aortic valve gradients (9.0 ± 3.4 and 17.0 ± 6.2 mm Hg, respectively) than conventional AVR patients (13.4 ± 5.5 and 24.2 ± 10.8 mm Hg, respectively; all $P < 0.001$). Patient-prosthesis mismatch was significantly less common with RDAVR than with AVR [overall: 16/66 (24.2%) vs 46/76 (60.5%); $P = 0.007$; severe: 2/66 (3.0%) vs 13/76 (17.1%)]. There were no significant differences between the RDAVR and AVR groups regarding 30-day safety endpoints. Survival rates in the RDAVR and conventional AVR groups were, respectively, 99.1% and 100.0% at 30 days, 97.1% and 95.1% at 1 year, and 93.3% and 94.1% at 3 years (P = nonsignificant). CONCLUSIONS In this retrospective study with matched populations, the RDAVR with the INTUITY valve system provided superior procedural and hemodynamic outcomes than a standard bioprosthesis without compromising safety.

DOI: https://doi.org/10.1097/IMI.0000000000000509

Outcomes of a Rapid Deployment Aortic Valve Versus Its Conventional Counterpart

A Propensity-Matched Analysis

Thorsten C.W. Wahlers, MD, Martin Andreas, MD,† Parwis Rahmanian, MD,* Pascal Candolfi, PhD,‡ Barbora Zemanova, MSc,‡ Christophe Giot, MD,‡ Enrico Ferrari, MD,§ and Günther Laufer, MD†*

Objective: The aim of this study was to compare outcomes after rapid-deployment aortic valve replacement (RDAVR) and conventional aortic valve replacement (AVR) from two studies.

Methods: Patients who underwent RDAVR (INTUITY valve) in the prospective, 5-year, single-arm multicenter TRITON study, or conventional AVR (Perimount Magna Ease valve) in the prospective Perimount Magna Ease postmarket study, were propensity score matched and compared for procedural, hemodynamic, safety, and clinical outcomes.

Results: Matched RDAVR (n = 106) and conventional AVR (n = 106) patients had similar baseline characteristics (mean ± SD age, 72.8 ± 7.6 vs 72.5 ± 7.4 years; male 59.4% vs 61.3%) and procedures (concomitant procedures: 41.5% vs 50.9%). Mean ± SD aortic cross-clamp time was significantly shorter in RDAVR than AVR patients (51.8 ± 20.9 vs 73.9 ± 33.2 minutes; $P < 0.001$), as was mean cardiopulmonary bypass time (82.8 ± 34.2 vs 102.4 ± 41.7 minutes; $P < 0.001$). At 1 year, RDAVR patients showed significantly lower mean ± SD and peak aortic valve gradients (9.0 ± 3.4 and 17.0 ± 6.2 mm Hg, respectively) than conventional AVR patients (13.4 ± 5.5 and 24.2 ± 10.8 mm Hg, respectively; all $P < 0.001$). Patient-prosthesis mismatch was significantly less common with RDAVR than with AVR [overall: 16/66 (24.2%) vs 46/76 (60.5%); $P = 0.007$; severe: 2/66 (3.0%) vs 13/76 (17.1%)]. There were no significant differences between the RDAVR and AVR groups regarding 30-day safety endpoints. Survival rates in the RDAVR and conventional AVR groups were, respectively, 99.1% and 100.0% at 30 days, 97.1% and 95.1% at 1 year, and 93.3% and 94.1% at 3 years (P = nonsignificant).

Conclusions: In this retrospective study with matched populations, the RDAVR with the INTUITY valve system provided superior procedural and hemodynamic outcomes than a standard bioprosthesis without compromising safety.

Key Words: Aortic valve replacement, Aortic valve stenosis, Rapid-deployment aortic valve replacement, Bioprosthetic valves.

(*Innovations* 2018;00:00–00)

Conventional aortic valve replacement (AVR) for aortic valve stenosis in patients older than 65 years is traditionally performed with standard bioprostheses requiring several U-fashion stitches or running sutures for the anchoring to the annulus. The new bioprosthetic valves allowing rapid-deployment aortic valve replacement (RDAVR) offer the potential for shorter aortic cross-clamp time and cardiopulmonary bypass (CPB) time, with shorter ventilation time and a similar survival rate when compared with conventional AVR.[1–8] Minimally invasive procedures for AVR (such as the partial upper ministernotomy or the right minithoracotomy) have been developed with the potential benefits of shortened intensive care unit and hospital stay, shorter ventilation time, and reduced blood loss.[9] However, the major drawback of these approaches is the longer cross-clamp time and CPB time due to the more complex surgical procedures.[9–12] Therefore, an RDAVR valve may be the ideal partner in minimally invasive aortic valve surgery.

The Edwards INTUITY valve system (Edwards Lifesciences, Irvine, CA USA) is a balloon-expandable, stented, bovine, pericardial bioprosthesis based on the Edwards Perimount valve system (Edwards Lifesciences, Irvine, CA USA).[2–7,13,14] A randomized controlled trial of minimally invasive RDAVR with INTUITY valves recently reported shorter cross-clamp time and improved hemodynamic function over 1 year versus conventional full sternotomy AVR.[6,7]

The aim of this study is to compare procedural, hemodynamic, safety, and midterm clinical outcomes (up to 3 years) of two matched populations operated for AVR with the INTUITY valve system and the standard Perimount Magna Ease valve.

Accepted for publication April 18, 2018.

From the *Department of Cardiac and Thoracic Surgery, Cologne University Heart Center, Cologne, Germany; †Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria; ‡Edwards Lifesciences SA, Nyon, Switzerland; and §Department of Cardiac Surgery, Cardiocentro Ticino, Lugano, Switzerland.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.innovjournal.com).

This study was sponsored by Edwards Lifesciences SA, Nyon, Switzerland.

Disclosures: Thorsten C.W. Wahlers, MD, and Martin Andreas, MD, report travel support from Edwards Lifesciences SA, Nyon, Switzerland. Parwis Rahmanian, MD, reports receiving lecture fees from Edwards Lifesciences SA, Nyon, Switzerland. Günther Laufer, MD, is a consultant for Edwards Lifesciences SA, Nyon, Switzerland. Pascal Candolfi, PhD, Barbora Zemanova, MSc, and Christophe Giot, MD, are employees of Edwards Lifesciences SA, Nyon, Switzerland. Enrico Ferrari, MD, declares no conflict of interest.

Address correspondence and reprint requests to Thorsten C.W. Wahlers, MD, Department of Cardiac and Thoracic Surgery, Cologne University Heart Center, Kerpener Str. 62, 50937 Köln, Germany. E-mail: thorsten.wahlers@uk-koeln.de.

ISSN: 1556-9845/18/0000–0000

METHODS

Study Design

This is a retrospective study comparing the outcome of patients operated for severe symptomatic aortic valve stenosis with RDAVR using the INTUITY valve system and included in the Surgical Treatment of Aortic Stenosis with an RDAVR Surgical Aortic Valve (TRITON) study with patients treated with conventional AVR using the Perimount Magna Ease valve included in a prospective postapproval study. Propensity scoring was used to generate two matched patient cohorts from these two studies.

Data Collection and Patients

TRITON (Clinicaltrials.gov NCT01445171) was a prospective, 5-year, single-arm, nonrandomized, multicenter trial conducted in Europe to evaluate the Edwards INTUITY valve (model 8300A or 8300AB), as previously described.[3–5] Briefly, recruited patients were male and female adults (aged ≥18 years) undergoing planned aortic valve surgery for aortic stenosis with or without aortic insufficiency, undertaken with or without concomitant procedures. Rapid-deployment aortic valve replacement was performed either through a minimal invasive access (upper ministernotomy or anterior right minithoracotomy) or through a full sternotomy, according to the surgeon's preference. Primary exclusion criteria included pure aortic insufficiency, concomitant valve disease requiring repair with an annuloplasty ring or replacement with prosthesis, left ventricular ejection fraction (LVEF) of less than 25%, true bicuspid aortic valve (ie, Sievers type 0), and myocardial infarction within 1 month or stroke within 6 months before the scheduled RDAVR. Clinical and echocardiographic follow-up data were collected at baseline, discharge, 3 months, and 12 months postoperatively and thereafter for 5 years. Hemodynamic assessments were made according to guidelines,[15] and all hemodynamic data were reviewed by an independent echocardiographic core laboratory (Columbia University Medical Center, New York, NY USA).

The Perimount Magna Ease postapproval study (ClinicalTrials.gov NCT01171625) was a prospective, single-arm, multicenter international study designed to assess the midterm safety and performance of the Perimount Magna Ease valve (model 3300TFX) in a postmarket, phase 4 setting. Based on the Carpentier-Edwards Perimount valve system, the Perimount Magna Ease valve is the conventional counterpart of the Edwards INTUITY valve. The Perimount Magna Ease valve has shown excellent clinical results and has been widely used.[16] The postmarketing study recruited male and female adults (aged ≥18 years) undergoing AVR with or without concomitant procedures. Patients were assessed at various time-points and signed informed consents. Both studies obtained respective institutional review board approvals before patient enrolment.[3,16] Both studies also used guidelines for reporting mortality and morbidity after cardiac valve interventions.[17]

Statistical Analysis

This retrospective analysis included all patients in the TRITON and Perimount Magna Ease postapproval studies who completed 3 years of follow-up. The analysis used an "as treated" approach, that is, excluding patients implanted with valves other than the INTUITY or the Perimount Magna Ease.

Preoperative data were compared between the groups using the independent samples *t* test for continuous variables and Pearson χ^2 test for discrete variables. Propensity scores, calculated from baseline variables, were used to match patients in two subgroups. A multivariable logistic regression model including all 35 preoperative risk factors available within both groups was applied (Supplementary Table S1, Supplemental Digital Content 1, http://links.lww.com/INNOV/A177). The C-statistic was 0.864, indicating good discrimination. Patient-to-patient matching was performed with the "Matching" library in the R Software (version 4.8-3.4)[18] using the nearest-neighbor matching without replacement algorithm, with a default caliper of 0.05 times the standard deviation (SD) of the logit of the propensity scores.

The covariance balance was assessed by calculating standardized mean difference and performing paired *t* test and McNemar test for continuous and discrete variables, respectively. Further, pseudo R^2 of the logistic regression model decreased from 0.329 on whole population to 0.067 on matched population. This shows that risk factors do not explain the participation probability after matching.

Baseline characteristics and postimplantation outcomes common to both studies were compared between the matched groups using the paired samples *t* test and McNemar tests for continuous and discrete variables, respectively. The Wilcoxon signed-rank test was used to compare mean valve sizes, after matching. Performance outcomes compared were cross-clamp and CPB times and 1-year hemodynamic variables, namely, LVEF, mean and peak aortic gradients, effective orifice area (EOA) and EOA indexed to patient body surface area (EOAi), and patient-prosthesis mismatch (PPM; measured using transthoracic echocardiography). Safety outcomes compared at 30 days after implantation included all-cause mortality, bleeding, major bleeding, endocarditis, valve explant, hemolysis, paravalvular leak, pacemaker implantation, structural and nonstructural valve deterioration, reoperation, thromboembolic event, valve thrombosis, cardiac failure, and renal, respiratory, and sternal wound complications. Two-sided tests were used throughout, and a type I error of 0.05 was considered significant. Kaplan-Meier survival curves for the two groups were compared using Cox regression, stratified by matched pairs. All analyses were performed using the R software (version 2.15.3).[19] All data are expressed as mean ± standard deviation (± SD) or as numbers and percentages (%).

RESULTS

Unmatched Group Characteristics

In the TRITON study, 287 of 295 patients enrolled in six centers in Germany and Austria between January 2010 and October 2012 received the Edwards INTUITY valve and completed a mean ± SD follow-up time of 2.7 ± 0.8 years. In the Perimount Magna Ease postapproval study, 258 patients were implanted with this valve between October 2007 and February 2013 and completed 3 years of follow-up. These populations were the basis for this analysis.

Before matching, patients in the RDAVR group (n = 287) were significantly older, more likely to be female, and generally sicker than patients in the conventional AVR group (n = 258) (Table 1). Rapid-deployment aortic valve replacement patients had more severe heart failure and were more likely to have

chronic renal failure, hypertension, arrhythmias (all $P < 0.001$), and diabetes ($P = 0.036$). Rapid-deployment aortic valve replacement patients also showed more concomitant mitral and tricuspid regurgitation than AVR patients ($P < 0.001$) and were more likely to have a pacemaker already implanted before surgery ($P = 0.005$).

Similar proportions of patients in the RDAVR and conventional AVR groups underwent isolated AVR (55.1% and

TABLE 1. Preoperative Baseline Characteristics of Patients Who Underwent RDAVR in the TRITON Study and Conventional AVR in the Perimount Magna Ease Postmarket Study, Before and After Propensity Score Matching

	Before Matching				After Matching			
	RDAVR (n = 287)*	Conventional AVR (n = 258)*	SMD	*P*†	RDAVR (n = 106)*	Conventional AVR (n = 106)*	SMD	*P*‡
Age, y	75.3 ± 6.7	68.5 ± 8.8	0.866	<0.001	72.8 ± 7.6	72.5 ± 7.4	0.049	0.660
Male sex	146 (50.9)	167 (64.7)	0.283	0.001	63 (59.4)	65 (61.3)	0.039	0.877
NYHA III + IV	151/283 (53.4)	82/252 (32.6)	0.430	<0.001	49 (46.2)	48 (45.3)	0.019	1
Body surface area, m^2	1.87 ± 0.19	1.96 ± 0.22	0.444	<0.001	1.91 ± 0.19	1.89 ± 0.20	0.073	0.614
Body mass index, kg/m^2	28.0 ± 4.3	28.9 ± 5.6	0.190	0.028	28.0 ± 4.1	27.6 ± 4.3	0.092	0.542
Concomitant diseases								
Coronary artery disease	139 (48.4)	106 (41.1)	0.148	0.102	50 (47.2)	55 (51.9)	0.094	0.583
Cardiomyopathy	7 (2.4)	5 (1.9)	0.034	0.916	6 (5.7)	4 (3.8)	0.089	0.752
Congestive heart failure	68 (23.7)	20 (7.8)	0.449	<0.001	9 (8.5)	9 (8.5)	<0.001	1
Mitral regurgitation	176 (61.3)	62 (24)	0.814	<0.001	42 (39.6)	43 (40.6)	0.019	1
Tricuspid regurgitation	115 (40.1)	39 (15.1)	0.581	<0.001	30 (28.3)	28 (26.4)	0.042	0.871
Myocardial infarction	13 (4.5)	13 (5)	0.024	0.938	5 (4.7)	7 (6.6)	0.082	0.752
Arrhythmias, any	97/286 (33.9)	36 (14)	0.481	<0.001	22 (20.8)	24 (22.6)	0.046	0.864
RBBB	13/286 (4.5)	2 (0.8)	0.236	0.016	2 (1.9)	2 (1.9)	<0.001	1
LBBB	16/286 (5.6)	9 (3.5)	0.101	0.334	3 (2.8)	4 (3.8)	0.053	1
Endocarditis	1 (0.3)	5 (1.9)	0.150	0.172	0 (0.0)	0 (0.0)	NA	NA
Dyslipidemia	157 (54.7)	163 (63.2)	0.173	0.055	63 (59.4)	64 (60.4)	0.019	1
History of rheumatic fever	0 (0)	5 (1.9)	0.199	0.055	0 (0.0)	3 (2.8)	0.241	0.248
Previous CABG	1 (0.3)	2 (0.8)	0.057	0.926	1 (0.9)	2 (1.9)	0.08	1
Previous PCI	23 (8)	12 (4.7)	0.138	0.154	4 (3.8)	6 (5.7)	0.089	0.752
Blood diatheses	6 (2.1)	1 (0.4)	0.154	0.167	2 (1.9)	1 (0.9)	0.08	1
Cancer	39 (13.6)	23 (8.9)	0.148	0.114	14 (13.2)	13 (12.3)	0.028	1
Chronic pulmonary disease	31 (10.8)	29 (11.2)	0.014	0.979	15 (14.2)	15 (14.2)	<0.001	1
Diabetes	86 (30)	56 (21.7)	0.190	0.036	26 (24.5)	21 (19.8)	0.114	0.499
Liver disease	15 (5.2)	7 (2.7)	0.129	0.204	3 (2.8)	6 (5.7)	0.141	0.505
Chronic renal failure	46 (16)	5 (1.9)	0.508	<0.001	9 (8.5)	5 (4.7)	0.152	0.386
Alcohol or drug abuse	3 (1)	5 (1.9)	0.074	0.611	2 (1.9)	2 (1.9)	<0.001	1
Atrial fibrillation/flutter	41/286 (14.3)	8 (3.1)	0.406	<0.001	9 (8.5)	7 (6.6)	0.071	0.789
TIA/CVA	10 (3.5)	15 (5.8)	0.111	0.274	3 (2.8)	2 (1.9)	0.062	1
Prior aortic valve surgery	0 (0)	2 (0.8)	0.125	0.433	0 (0.0)	0 (0.0)	NA	NA
AV block I	15/286 (5.2)	6 (2.3)	0.153	0.123	3 (2.8)	5 (4.7)	0.099	0.724
Pacemaker	13 (4.5)	1 (0.4)	0.270	0.005	0 (0.0)	1 (0.9)	0.138	1
Smoking, previous	54 (18.8)	96 (37.2)	0.418	<0.001	29 (27.4)	20 (18.9)	0.202	0.222
Smoking, current	16 (5.6)	16 (6.2)	0.027	0.898	6 (5.7)	10 (9.4)	0.143	0.453
Hypertension	249 (86.8)	171 (66.3)	0.498	<0.001	82 (77.4)	83 (78.3)	0.023	1
Surgical procedures			0.221	0.087			0.268	0.395
Isolated AVR	158 (55.1)	144 (55.8)			62 (58.5)	52 (49.1)		
AVR + CABG	78 (27.2)	51 (19.8)			29 (27.4)	29 (27.4)		
AVR + non-CABG	38 (13.2)	43 (16.7)			11 (10.4)	16 (15.1)		
AVR + CABG + other	13 (4.5)	20 (7.8)			4 (3.8)	9 (8.5)		

Variables are presented as mean ± SD or number and percentage (%).

*Denominator unless otherwise shown.

†Independent samples *t* test for continuous variables, Pearson χ^2 test for categorical variables.

‡Paired samples *t* test for continuous variables, McNemar test for categorical variables.

AV block, atrioventricular block; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CVA, cerebrovascular accident; LBBB, left bundle branch block; NA, not applicable; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; RBBB, right bundle branch block; RDAVR, rapid deployment AVR; SMD, standardized mean difference; TIA, transient ischemic attack.

TABLE 2. Intraoperative Procedural Times in the Matched RDAVR and AVR Groups

Procedure Group and Time Variable	RDAVR	Conventional AVR	*P*
All patients	n = 106	n = 106	
AXC, min	51.8 ± 20.9	73.9 ± 33.2	<0.001
CPB, min	82.8 ± 34.2	102.4 ± 41.7	<0.001
Isolated AVR	n = 62	n = 52	
AXC, min	45 ± 18.7	64.6 ± 20.7	<0.001
CPB, min	71.4 ± 27.5	87.2 ± 24.0	0.001
AVR + CABG	n = 29	n = 29	
AXC, min	63.6 ± 20	97.1 ± 46.3	<0.001
CPB, min	102.3 ± 35	131.7 ± 56.6	0.022
AVR + non-CABG	n = 11	n = 16	
AXC, min	48.7 ± 13.8	60.6 ± 22.5	0.101
CPB, min	80.1 ± 33.3	97.1 ± 35.9	0.22
AVR + CABG + other	n = 4	n = 9	
AXC, min	80.2 ± 18.9	75.1 ± 19.5	0.67
CPB, min	126.2 ± 38.6	104.2 ± 26.3	0.354

Data are presented as mean ± SD or numbers and percentage (%).

P values from paired samples *t* test for analysis of all patients; independent samples *t* test for subgroups.

AVR, aortic valve replacement; AXC, aortic cross-clamp; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; RDAVR, rapid deployment AVR.

55.8%, respectively), AVR plus coronary artery bypass grafting (CABG) (27.2% and 19.8%), AVR plus a non-CABG procedure (13.2% and 16.7%), or AVR plus CABG and at least one additional procedure (4.5% and 7.8%). The mean ± SD implanted valve size was 23.1 ± 1.9 mm in the RDAVR group and 23.7 ± 2.2 mm in the conventional AVR group ($P < 0.001$).

Before matching, the mean ± SD propensity score was 0.72 ± 0.24 in the RDAVR group (n = 282; data missing for 5 patients) and 0.32 ± 0.25 in the conventional AVR group (n = 252; data missing for 6 patients).

Matched Group Characteristics

Propensity score matching resulted in two similar groups, each comprising 106 patients. The mean ± SD propensity scores for the matched RDAVR and conventional AVR groups were 0.52 ± 0.23 and 0.52 ± 0.23, respectively.

The matched RDAVR and conventional AVR groups showed similar baseline characteristics, as shown by standardized mean differences of less than 0.1 for most variables (Table 1). In addition, there is no significant difference in risk factors between the two groups as tested by paired *t* test and McNemar test, respectively. Similar proportions of matched RDAVR and conventional AVR patients underwent isolated AVR (58.5% vs 49.1%, respectively), AVR plus CABG (27.4% and 27.4%), AVR and a non-CABG procedure (10.4% and 15.1%), or AVR plus CABG and at least one additional procedure (3.8% and 8.5%). The mean implanted valve size was 23.4 ± 1.8 mm in the RDAVR group and 23.0 ± 2.3 mm in the conventional AVR group ($P = 0.217$). The remaining results refer exclusively to the matched groups.

Procedural Outcomes

Mean ± SD aortic cross-clamp time was significantly shorter in the matched RDAVR group (51.8 ± 20.9 minutes) than in the AVR group (73.9 ± 33.2 minutes; $P < 0.001$), as was the CPB time (82.8 ± 34.2 minutes vs 102.4 ± 41.7 minutes; $P < 0.001$). Cross-clamp and CPB times were significantly shorter in the RDAVR group versus the conventional AVR cohorts also in the largest subgroups of patients undergoing isolated AVR and AVR plus CABG (Table 2).

The distribution of the surgical approach for the INTUITY arm after matching was full sternotomy 75.5% (80/106), mini-upper sternotomy 19.8% (21/106), and right thoracotomy 4.7% (5/106). Please note that surgical approach data are not available for Magna Ease arm.

Valve Hemodynamic Performance at Follow-up

At 1-year follow-up, patients who underwent RDAVR showed lower mean ± SD and peak valve gradients (9.0 ± 3.4 mm Hg and 17.0 ± 6.2 mm Hg, respectively) than those who underwent conventional AVR (13.4 ± 5.5 mm Hg and 24.2 ± 10.8 mm Hg, respectively; $P < 0.001$ for both comparisons) (Table 3). Mean and peak gradients were significantly lower in the RDAVR cohort for patient subgroups implanted with 21-, 23-, and 25-mm valves. The same pattern of results was seen in the 19 mm and 27 mm subgroups, although statistical significance was not achieved in these small groups (Supplementary Tables S2–S6, Supplemental Digital Content 2, http://links.lww.com/INNOV/A190). Moderate-to-severe PPM was significantly less common in the RDAVR group (overall 16/66; 24.2%) than the conventional AVR group (46/76; 60.5%; $P = 0.007$). Moderate PPM (EOAi, 0.65–0.85 cm^2/m^2) was observed in 21.2% of the RDAVR group and 43.4% of the conventional AVR groups, respectively, whereas severe PPM (EOAi, <0.65 cm^2/m^2) occurred in 3.0% and 17.1% of the cohorts, respectively (Table 3). Patient-prosthesis mismatch was less common with RDAVR in each valve size subgroup (Supplementary Tables S2–S6, Supplemental Digital Content 2, http://links.lww.com/INNOV/A190). The difference reached

TABLE 3. Valve Hemodynamic Variables at 1 Year Postimplant in the Matched RDAVR and Conventional AVR Groups

Variable	RDAVR	Conventional AVR	*P*
Aortic gradient, mm Hg	n = 84	n = 84	
	9.0 ± 3.4	13.4 ± 5.5	<0.001
Peak aortic gradient, mm Hg	n = 84	n = 84	
	17.0 ± 6.2	24.2 ± 10.8	<0.001
EOA, cm	n = 74	n = 76	
	1.7 ± 0.2	1.6 ± 0.4	0.120
EOAi, cm^2/m^2	n = 66	n = 76	
	0.9 ± 0.1	0.8 ± 0.2	0.070
Patient-prosthesis mismatch	n = 66	n = 76	0.007
Moderate (EOAi 0.65–0.85 cm^2/m^2)	14 (21.2)	33 (43.4)	
Severe (EOAi <0.65 cm^2/m^2)	2 (3.0)	13 (17.1)	
LVEF, %	n = 59	n = 82	
	65.1 ± 8.3	62.1 ± 7.5	0.146

Data are presented as mean ± SD or numbers and percentage (%).

P values from paired samples *t* test for continuous variables, McNemar for prosthesis-patient mismatch.

AVR, aortic valve replacement; EOA, effective orifice area; EOAi, index effective orifice area; LVEF, left ventricular ejection fraction; RDAVR, rapid deployment AVR.

TABLE 4. Safety Outcomes in the Matched RDAVR and Conventional AVR Groups at 30 Days After Implantation

Outcome	RDAVR (n = 106)	Conventional AVR (n = 106)	*P*
Mortality	1 (0.9)	0 (0)	1
Bleeding	13 (12.3)	4 (3.8)	0.052
Major bleeding	11 (10.4)	3 (2.8)	0.061
Endocarditis	0 (0)	0 (0)	NA
Valve explant	2 (1.9)*	1 (0.9)	1
Paravalvular leak (degree 1–2)	2 (1.9)	0 (0)	0.48
Major paravalvular leak (degree 3–4)	2 (1.9)	0 (0)	0.48
Reoperation†	2 (1.9)	1 (0.9)	1
Structural valve deterioration	0 (0)	0 (0)	NA
Nonstructural valve deterioration	0 (0)	0 (0)	NA
Permanent pacemaker implantation	7 (6.6)	4 (3.8)	0.546
Thromboembolic events	4 (3.8)	3 (2.8)	1
Valve thrombosis	0 (0)	0 (0)	NA
Heart failure	1 (0.9)	1 (0.9)	1
Acute kidney failure	7 (6.6)	1 (0.9)	0.077
Respiratory failure/pneumonia	5 (4.7)	5 (4.7)	1
Sternal wound complications	4 (3.8)	5 (4.7)	1

Data are presented as numbers and percentage (%).

P values from McNemar test.

*See Kocher et al[3] for details.

†The reasons for reoperation were specified as moderate paravalvular leak (n = 1) and bleeding-hemolysis (n = 1) in the RDAVR group and "other, not specified" in the AVR group (n = 1).

AVR, aortic valve replacement; NA, not applicable; RDAVR, rapid deployment AVR.

statistical significance in the largest 23-mm valve subgroup: moderate PPM occurred in 3/27 (11.1%) of these RDAVR patients (no severe episodes), whereas in the conventional AVR subgroup there were 13 patients (46.4%) with moderate PPM and 5 patients (17.9%) with severe PPM (overall $P < 0.001$). Left ventricular ejection fraction did not differ significantly between the groups.

Clinical Safety Outcomes

The matched RDAVR and conventional AVR groups did not differ significantly with respect to 30-day safety endpoints (Table 4) or 3-year Kaplan-Meier survival curves (Fig. 1). This was the case for patients in each subgroup categorized by the procedure type, that is, isolated AVR, AVR plus CABG, AVR plus non-CABG, and AVR plus CABG and another procedure (Supplementary Tables S7–S10, Supplemental Digital Content 3, http://links.lww.com/INNOV/A191). It should be noted that RDAVR group did have numerically higher numbers of patients with major bleeding, major paravalvular leak, permanent pacemaker implantations, and acute kidney failure (Table 4). Estimated survival rates in the RDAVR and conventional AVR groups were, respectively, 99.1% vs 100.0% at 30 days, 97.1% vs 95.1% at 1 year, 93.3% vs 95.1%, at 2 years, and 93.3% vs 94.1% at 3 years (Fig. 1).

DISCUSSION

This propensity-matched analysis showed that patients who underwent RDAVR with the INTUITY valve system had significantly shorter aortic cross-clamp and CPB times, lower mean and peak aortic valve gradients, lower risk of moderate or severe PPM, and similar safety and survival rates over 3 years, as compared with patients who underwent conventional AVR with standard Perimount valves. Although this was a retrospective analysis, propensity score matching rendered two well-matched cohorts of patients that did not differ significantly according to a battery of preoperative variables and which were therefore suitable for comparison. Propensity score matching is a powerful statistical tool to strengthen causal inferences drawn from retrospective studies and to ensure that only similar patients are selected. It is increasingly used and accepted in the literature, most notably for medical devices where randomized controlled

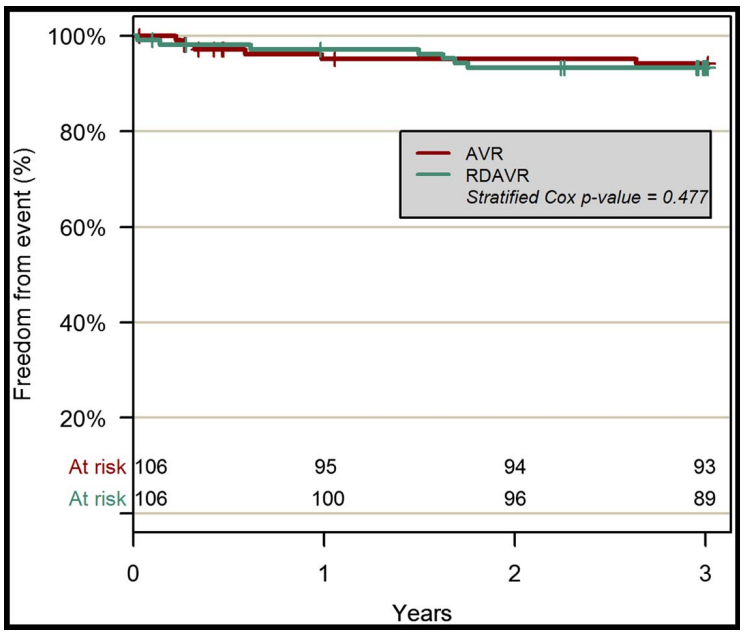

FIGURE 1. Kaplan-Meier survival curves for the matched cohorts after rapid-deployment aortic valve replacement (RDAVR; Edwards INTUITY) and conventional aortic valve replacement (AVR; Perimount Magna Ease).

trials are more challenging to perform and real-world evidence can be more powerful.[20,21] These results add to a growing body of evidence suggesting that RDAVR offers procedural benefits and improved hemodynamics compared with conventional aortic bioprostheses. Experts have recently recommended that sutureless and rapid deployment valves should be considered as the prosthesis of choice for isolated aortic valve procedures in patients with comorbidities, in the elderly, and in certain other circumstances such as complex concomitant procedures requiring longer surgical time.[22]

The aortic cross clamp time and CPB time are predictors of mortality, morbidity, and length of hospital stay in patients undergoing AVR.[10–12] The procedural times for conventional AVR in the present analysis are consistent with reported ranges in the available literature.[2,23–25] In this analysis, RDAVR was associated with significantly reduced cross-clamp and CPB times overall and, in particular, in the subgroups who underwent AVR only or AVR plus CABG. A systematic review of 11 studies using three different valve products recently concluded that RDAVR was invariably associated with shorter aortic cross-clamp times than conventional AVR (30–56 minutes vs 49–88 minutes).[1] Most of these studies were cohort studies, but the findings were confirmed by the prospective, randomized, multicenter CADENCE-MIS study. CADENCE-MIS compared minimal invasive RDAVR (using the INTUITY aortic valve system without concomitant procedures; n = 46) versus AVR via full sternotomy using a conventional stented valve of the investigator's preference (n = 48).[6,7] Minimal invasive RDAVR was associated with significantly reduced cross-clamp times compared with conventional AVR (41.3 ± 20.3 minutes vs 54.0 ± 20.3 minutes; $P < 0.001$), although CPB time was not significantly shortened. Supporting results were also provided by a single-center, parallel cohort study that compared RDAVR with the INTUITY valve (n = 116) versus conventional AVR with Perimount Magna Ease (n = 132).[2] Patients were neither randomized nor matched in this study, and the mean ± SD valve size was significantly higher in the conventional AVR group than RDAVR group (23.2 ± 2.0 mm vs 22.5 ± 2.2 mm; $P = 0.007$). Minimal invasive procedures were significantly more common among patients implanted with the RDAVR valve than conventional valve (59% vs 39%; $P < 0.001$) and, although cross-clamp times were similar between the groups overall, RDAVR was associated with reduced cross-clamp time, perfusion, and procedural times versus conventional AVR in patients who underwent full sternotomy.[2] Recently, a propensity-matched, single-center study (n = 41 pairs) also confirmed that RDAVR was associated with significantly shorter cross-clamp time (71 ± 33 minutes vs 106 ± 42 minutes; $P < 0.01$) and CPB times (95 ± 42 minutes vs 134 ± 47 minutes; $P < 0.01$) than conventional AVR, when both types of prosthesis were implanted through a full sternotomy.[8] In this analysis, RDAVR was also associated with significantly lower rates of moderate and severe PPM at 1 year versus conventional AVR, together with lower mean and peak transvalvular gradients.

Patient-prosthesis mismatch occurs when the EOA of the bioprosthesis is too small compared with the patient's body size, causing a high transvalvular gradient and lower long-term survival.[26–28] Our findings are consistent with previously reported studies. In the CADENCE-MIS, minimal invasive RDAVR patients also had significantly lower peak gradients after 1 year, with a trend toward lower mean gradients, and a significantly greater EOA compared with the control group.[7] In the aforementioned parallel cohort study,[2] the subgroup analysis of the most common valve sizes (21 mm and 23 mm; implanted in 64% of patients) also showed significantly lower mean postoperative transvalvular gradients in the RDAVR group than the conventional AVR group. Moreover, the aforementioned multiproduct systematic review reported benefits of RDAVR on postoperative bleeding, blood transfusion requirements, ventilation time, and renal injury.[1] Another recent propensity-matched, single-center study (n = 41 pairs) showed significant benefits of RDAVR over conventional AVR on mean ± SD ventilation time (17 ± 25 hours vs 63 ± 131 hours; $P < 0.01$), intensive care unit stay (51 ± 45 hours vs 108 ± 157 hours; $P = 0.03$), and new onset of postoperative atrial fibrillation/flutter (8% vs 20%; $P = 0.02$).[8]

In the present analysis, we found no significant differences between the matched RDAVR and conventional AVR groups with respect to safety endpoints assessed at 30 days postimplant, including new permanent pacemaker implantation. The 3-year Kaplan-Meier survival rates were also good and similar between the cohorts. These data support previous evidence that mortality rates with RDAVR are similar to those with conventional AVR.[1,2,7,8] Further real-world evidence regarding longer-term outcomes after RDAVR is awaited from ongoing registry studies.[29,30]

There are some limitations with this study; this was a retrospective analysis of data over a 6-year period from two separate studies with differing protocols and available datasets. Studies of this type are inherently subject to a significant risk of bias, including allocation bias associated with surgeon preference and classification bias arising from data collection and recording. Therefore, the propensity score matching was used to create comparable cohorts from these studies. Although the matched cohorts did not differ significantly according to available data, the potential for additional, untested confounding variables to introduce bias cannot be fully excluded. The analysis was also limited to the outcomes variables for which data were available, at common timepoints, from both studies. Pertinent data that may have been informative, but which were unavailable from at least one study, included the surgical approach and the left ventricular mass regression. This study was specifically designed to compare cohorts implanted with the INTUITY and the Perimount Magna Ease valve and therefore rates of conversion from the INTUITY valve to conventional valve (eg, because of severe paravalvular leak) were not analyzed. However, there were no significant differences in paravalvular leak rates between the two cohorts. Finally, our analysis was limited to 3-year follow-up and a longer follow-up might be necessary to unmask potential survival benefit with the RDAVR valve.

In conclusion, in this multicentric, retrospective analysis of matched populations, the RDAVR using the INTUITY valve system provided superior procedural and hemodynamic outcomes compared with the conventional AVR with the Perimount Magna Ease valve, without compromising safety.

ACKNOWLEDGMENTS

Lee Baker (Zenith Healthcare Communications Ltd, Chester, United Kingdom) provided editorial assistance in the development of this article, funded by Edwards Lifesciences SA, Nyon, Switzerland.

REFERENCES

1. Davies RA, Bandara TD, Perera NK, et al. Do rapid deployment aortic valves improve outcomes compared with surgical aortic valve replacement? *Interact Cardiovasc Thorac Surg*. 2016;23:814–820.
2. Andreas M, Wallner S, Habertheuer A, et al. Conventional versus rapid-deployment aortic valve replacement: a single-centre comparison between the Edwards Magna valve and its rapid-deployment successor. *Interact Cardiovasc Thorac Surg*. 2016;22:799–805.
3. Kocher AA, Laufer G, Haverich A, et al. One-year outcomes of the Surgical Treatment of Aortic Stenosis With a Next Generation Surgical Aortic Valve (TRITON) trial: a prospective multicenter study of rapid-deployment aortic valve replacement with the EDWARDS INTUITY Valve System. *J Thorac Cardiovasc Surg*. 2013;145:110–115.
4. Haverich A, Wahlers TC, Borger MA, et al. Three-year hemodynamic performance, left ventricular mass regression, and prosthetic-patient mismatch after rapid deployment aortic valve replacement in 287 patients. *J Thorac Cardiovasc Surg*. 2014;148:2854–2860.
5. Wahlers TC, Haverich A, Borger MA, et al. Early outcomes after isolated aortic valve replacement with rapid deployment aortic valve. *J Thorac Cardiovasc Surg*. 2016;151:1639–1647.
6. Borger MA, Moustafine V, Conradi L, et al. A randomized multicenter trial of minimally invasive rapid deployment versus conventional full sternotomy aortic valve replacement. *Ann Thorac Surg*. 2015;99:17–25.
7. Borger MA, Dohmen PM, Knosalla C, et al. Haemodynamic benefits of rapid deployment aortic valve replacement via a minimally invasive approach: 1-year results of a prospective multicentre randomized controlled trial. *Eur J Cardiothorac Surg*. 2016;50:713–720.
8. Smith AL, Shi WY, Rosalion A, et al. Rapid-deployment versus conventional bio-prosthetic aortic valve replacement. *Heart Lung Circ*. 2017;26:187–193.
9. Brown ML, McKellar SH, Sundt TM, et al. Ministernotomy versus conventional sternotomy for aortic valve replacement: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg*. 2009;137:670–679.
10. Salis S, Mazzanti VV, Merli G, et al. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22:814–822.
11. Nissinen J, Biancari F, Wistbacka JO, et al. Safe time limits of aortic cross-clamping and cardiopulmonary bypass in adult cardiac surgery. *Perfusion*. 2009;24:297–305.
12. Al-Sarraf N, Thalib L, Hughes A, et al. Cross-clamp time is an independent predictor of mortality and morbidity in low- and high-risk cardiac patients. *Int J Surg*. 2011;9:104–109.
13. Merk DR, Lehmann S, Holzhey DM, et al. Minimal invasive aortic valve replacement surgery is associated with improved survival: a propensity-matched comparison. *Eur J Cardiothorac Surg*. 2015;47:11–17.
14. Borger MA. Minimally invasive rapid deployment Edwards Intuity aortic valve implantation. *Ann Cardiothorac Surg*. 2015;4:193–195.
15. Hage FG, Nanda NC. American Society of Echocardiography's Guidelines and Standards Committee; American College of Cardiology; American Heart Association; European Association of Echocardiography; Japanese Society of Echocardiography; Canadian Society of Echocardiography. Guidelines for the evaluation of prosthetic valves with echocardiography and Doppler ultrasound: value and limitations. *Echocardiography*. 2010;27:91–93.
16. Wyss TR, Bigler M, Stalder M, et al. Absence of prosthesis-patient mismatch with the new generation of Edwards stented aortic bioprosthesis. *Interact Cardiovasc Thorac Surg*. 2010;10:884–887.
17. Akins CW, Miller DC, Turina MI, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. *J Thorac Cardiovasc Surg*. 2008;135:732–738.
18. Sekhon JS. Multivariate and propensity score matching software with automated balance optimization: the Matching package for R. *J Stat Softw*. 2011;42:1–52. Version 4.8-3.4. Available at: https://libraries.io/cran/Matching/4.8-3.4.
19. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2013. Available at: https://cran.r-project.org/manuals.html.
20. Ventola CL. Challenges in evaluating and standardizing medical devices in health care facilities. *P T*. 2008;33:348–359.
21. Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs—same or different? *Value Health*. 2009;12:402–404.
22. Gersak B, Fischlein T, Folliguet TA, et al. Sutureless, rapid deployment valves and stented bioprosthesis in aortic valve replacement: recommendations of an International Expert Consensus Panel. *Eur J Cardiothorac Surg*. 2016;49:709–718.
23. Dalmau MJ, María González-Santos J, López-Rodríguez J, et al. One year hemodynamic performance of the Perimount Magna pericardial xenograft and the Medtronic Mosaic bioprosthesis in the aortic position: a prospective randomized study. *Interact Cardiovasc Thorac Surg*. 2007;6:345–349.
24. Dewey TM, Herbert MA, Ryan WH, et al. Influence of surgeon volume on outcomes with aortic valve replacement. *Ann Thorac Surg*. 2012;93:1107–1112.
25. Bobiarski J, Newcomb AE, Elhenawy AM, et al. One-year hemodynamic comparison of Perimount Magna with St Jude Epic aortic bioprostheses. *Arch Med Sci*. 2013;9:445–451.
26. Head SJ, Mokhles MM, Osnabrugge RL, et al. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years. *Eur Heart J*. 2012;33:1518–1529.
27. Dayan V, Vignolo G, Soca G, et al. Predictors and outcomes of prosthesis-patient mismatch after aortic valve replacement. *JACC Cardiovasc Imaging*. 2016;9:924–933.
28. Mannacio V, Mannacio L, Mango E, et al. Severe prosthesis-patient mismatch after aortic valve replacement for aortic stenosis: analysis of risk factors for early and long-term mortality. *J Cardiol*. 2017;69:333–339.
29. Di Eusanio M, Phan K, Bouchard D, et al. Sutureless Aortic Valve Replacement International Registry (SU-AVR-IR): design and rationale from the International Valvular Surgery Study Group (IVSSG). *Ann Cardiothorac Surg*. 2015;4:131–139.
30. Bautista-Hernandez V, Cal-Purriños N, Arribas-Leal JM, et al. Rapid Deployment Aortic Replacement (RADAR) Registry in Spain: a protocol. *BMJ Open*. 2017;7:e011437.

CLINICAL PERSPECTIVE

This propensity-matched analysis compared patients who underwent implantation of the Edwards Lifesciences rapid-deployment INTUITY valve (RDAVR) during the prospective multicenter TRITON study, to those who underwent conventional AVR with a Perimount Magna Ease valve in a prospective postmarket study. One hundred six propensity-matched patients in each group were compared. They had similar baseline characteristics. The mean cross-clamp time was significantly shorter in the RDAVR group as was mean cardiopulmonary bypass time. At 1 year, RDAVR patients had significantly lower mean and peak aortic valve gradients. There was no difference in 30-day safety endpoints and no difference in survival. The authors concluded that RDAVR with the INTUITY valve system provided superior procedural and hemodynamic outcomes, without compromising safety.

This is an interesting propensity-matched retrospective analysis that adds further data to support the use of rapid deployment valves. However, this study has significant limitations. It was a retrospective analysis and was not a randomized trial. Most importantly, the relatively small number of matched patients in each group left it underpowered to detect what might have been important differences. With these limitations in mind, shorter operative times and better valve hemodynamics were shown to be advantages of rapid-deployment valves.

